

Discontinuation of Isolation Precaution in COVID Patients

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Objectives

- Example of cases
- Is it really safe to discontinue isolation precaution?
 - What are evidence?
 - Should we follow up RT-PCR for COVID-19?
- What additional measures that we need to do?


Rationale

- COVID-19 cases are increasing
- Increasing cases occurs mainly due to the influx of patients (refer, active case detection) > patients that we can refer to field hospital
- TU field hospital is now closed and it is very difficult to refer cases out to other field hospitals
- Most patients are chronically ill with multiple underlying diseases, older age and require time to recover. Most have no active medical issues.

Rational

- Severe cases have been referred to ICUs at TUH without extra precaution
- No safety concern at ICU, once culture is established
- Treatment in cohort unit associated with poor outcomes that might result in increasing in mortality

High mortality in coronavirus disease 2019 (COVID-19)–suspect unit Lessons learned for patient safety

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Table 1. Comparison of 78 Patients Admitted to COVID-19 Suspect Unit, by In-Hospital Mortality

Variable	Total (n = 78)	Died (n = 10)	Survived (n = 68)	P Value
Age, median y (range)	40.5 (15–70.5)	55 (15–70.5)	37 (27–59)	0
Sex, female	36 (46)	6 (60)	32 (47.1)	0.74
Underlying comorbidities				
Hypertension	12 (15.4)	3 (25)	9 (13.2)	0.17
Diabetes	10 (12.8)	2 (20)	8 (11.8)	0.60
Lung disease	8 (10.3)	1 (10)	7 (10.3)	1
Heart disease	5 (6.4)	3 (30)	2 (2.9)	0.02
Kidney disease	3 (3.8)	0 (0)	3 (4.4)	1
Initial evaluation site				
Emergency department	40 (51.3)	10 (100)	30 (44)	0.001
Emerging infectious diseases unit	29 (37.2)	0 (0)	29 (42.6)	0.01
Outpatient department	9 (11.5)	0 (0)	9 (13.2)	0.59
Delay processes of care				
Laboratory procurement ^a	28 (29.5)	6 (60)	22 (32)	0.09
Time to admission ^b	49 (39.7)	5 (50)	44 (65)	0.36
Critical clinical management ^c	4 (5.1)	4 (40)	0 (0)	<.001
Final diagnosis				
Infectious diseases				
Viral infection ^d	34 (43.6)	0 (0)	34 (50)	0.004
Bacterial infections	29 (37.2)	9 (90)	20 (29.4)	<.001
Fungal infections	4 (5.1)	0 (0)	4 (5.9)	0.57
Noninfectious diseases ^e				
	12 (15.4)	2 (20)	10 (14.7)	0.19

Example of cases

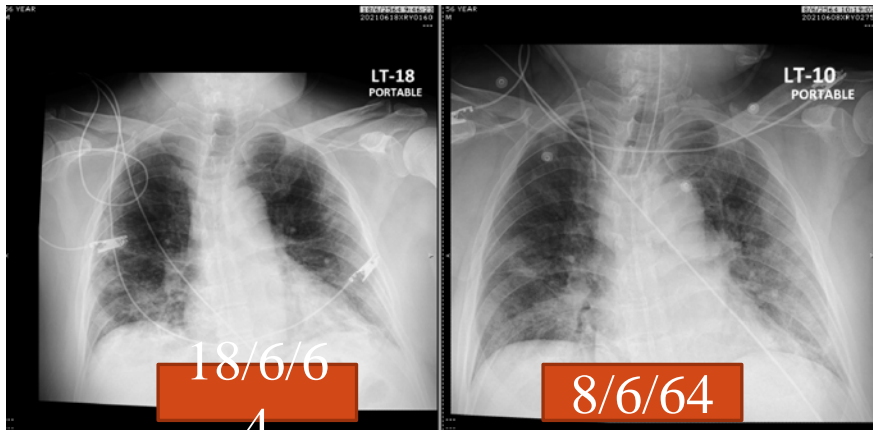
Cohort cases

Male 56 yrs old

U/D : HT, asthma

Dx : Covid-19 pneumonia

DOI : 18 (onset 2/6/64)



O2 Canula 3 LPM

Case 1: Ward ยท 1 Bed 5

A 85 year-old Thai male, HT-BPH-GERD, non-smoker, no-occupied person

Risk factor: ภรรยาและลูกสาวติดเชื้อ COVID-19 (22/5/64)

Dx: mild-moderate COVID-19 pneumonia with risk for severe disease (age > 60 yrs)

Symptoms onset: 13/5/64

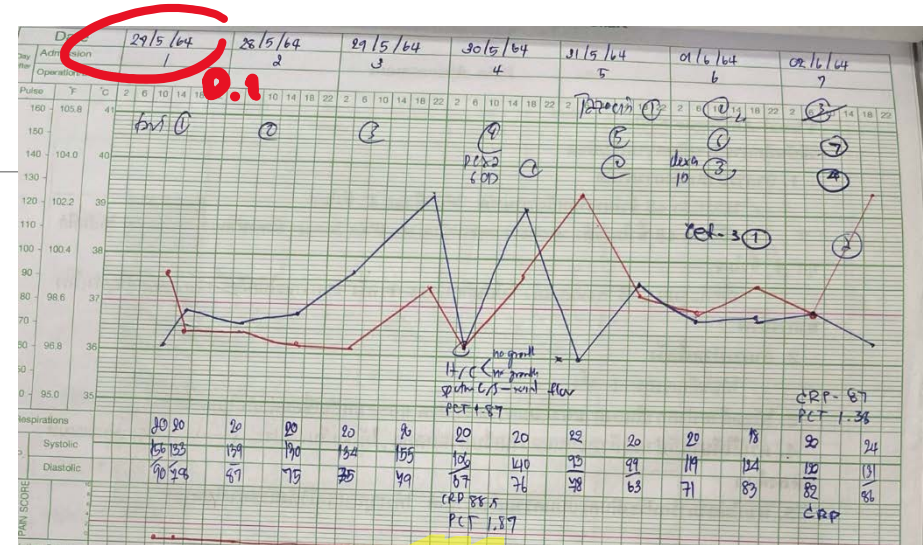
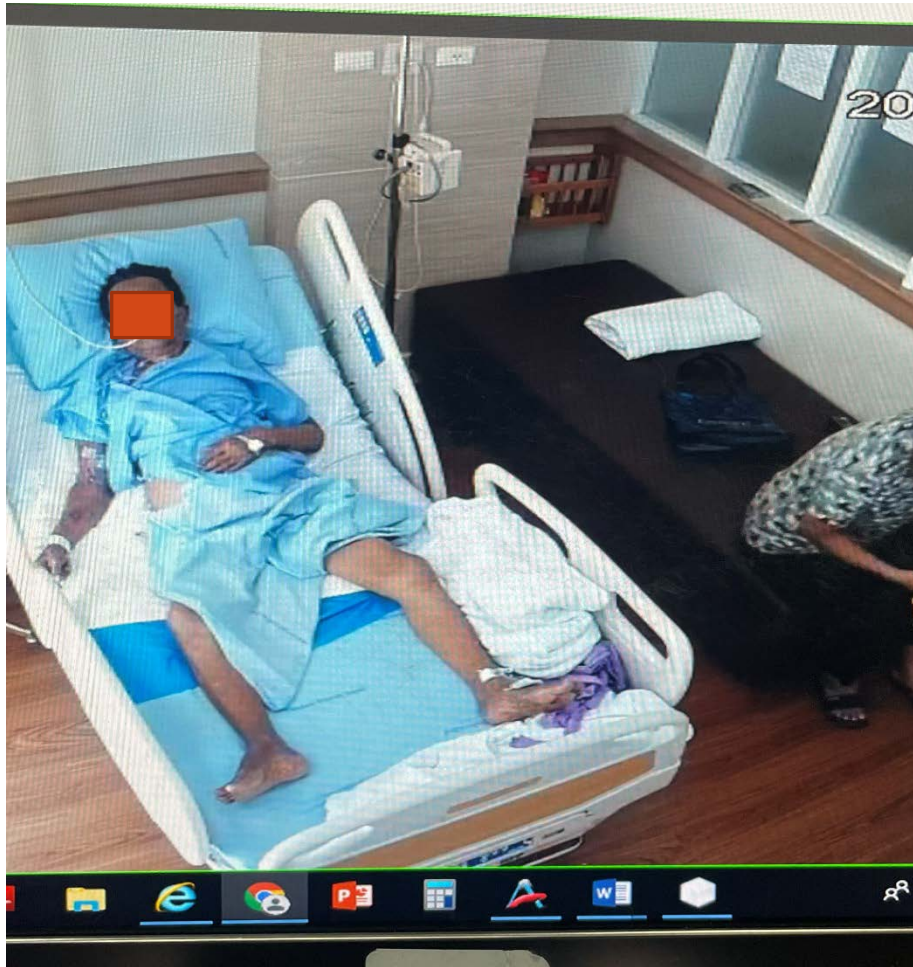
Swab COVID-19 +ve: 26/5/64

Admit 27/5/64 (Cohort) >> Transfer to RCU 5/6/64 >> Transfer to ยท1 13/6/64

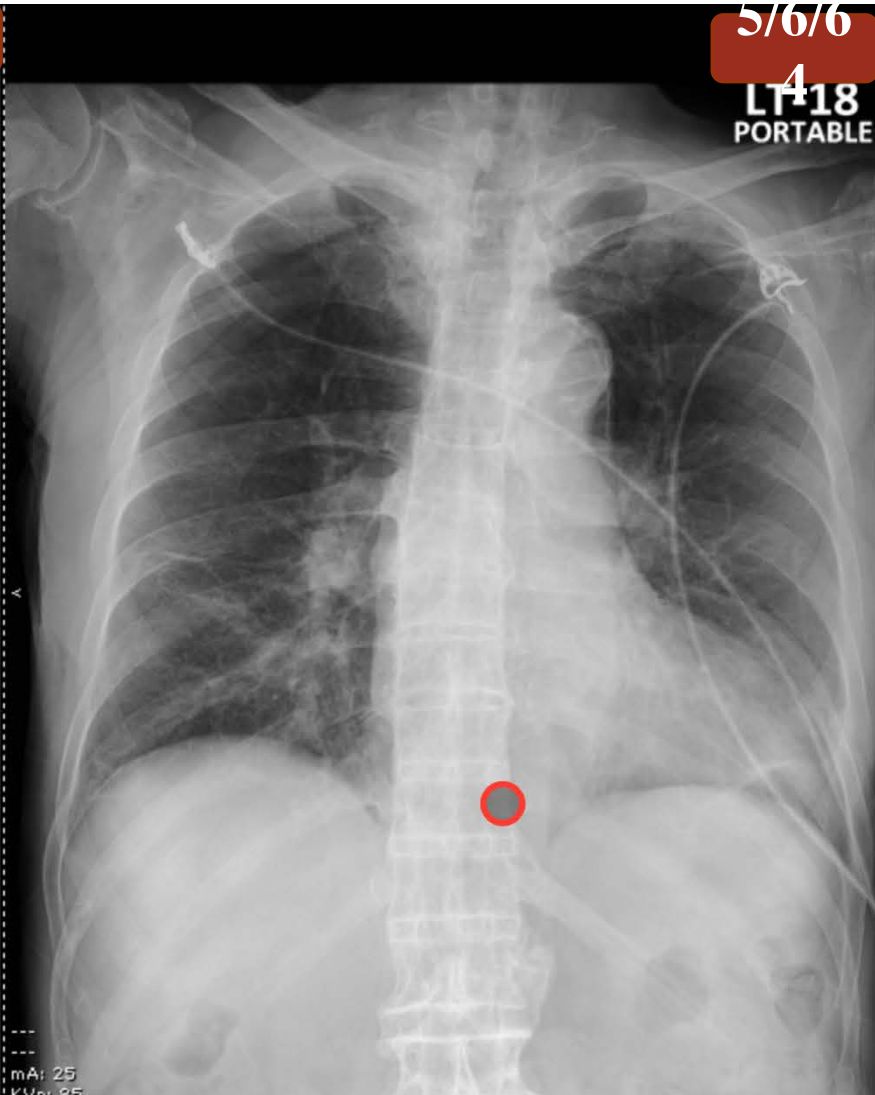
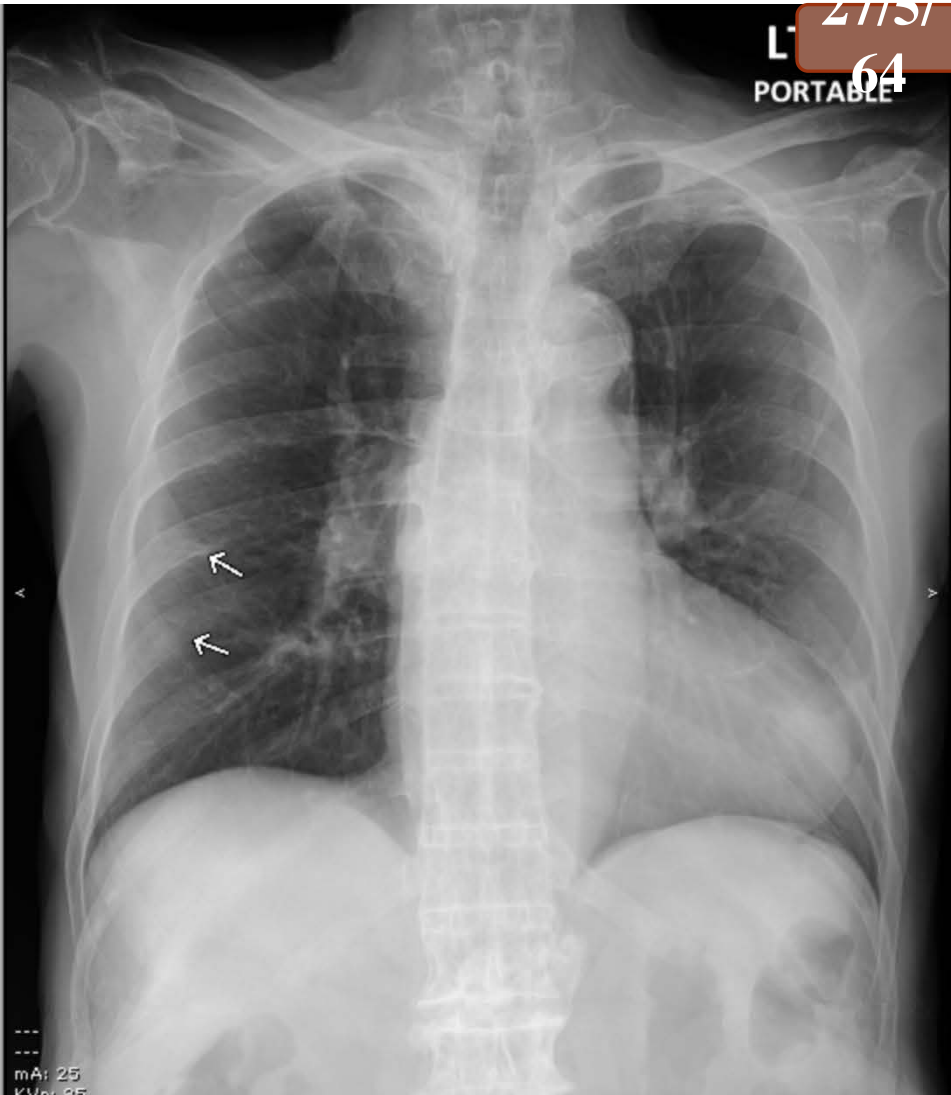
Case 1: Ward ยพ 1 Bed 5

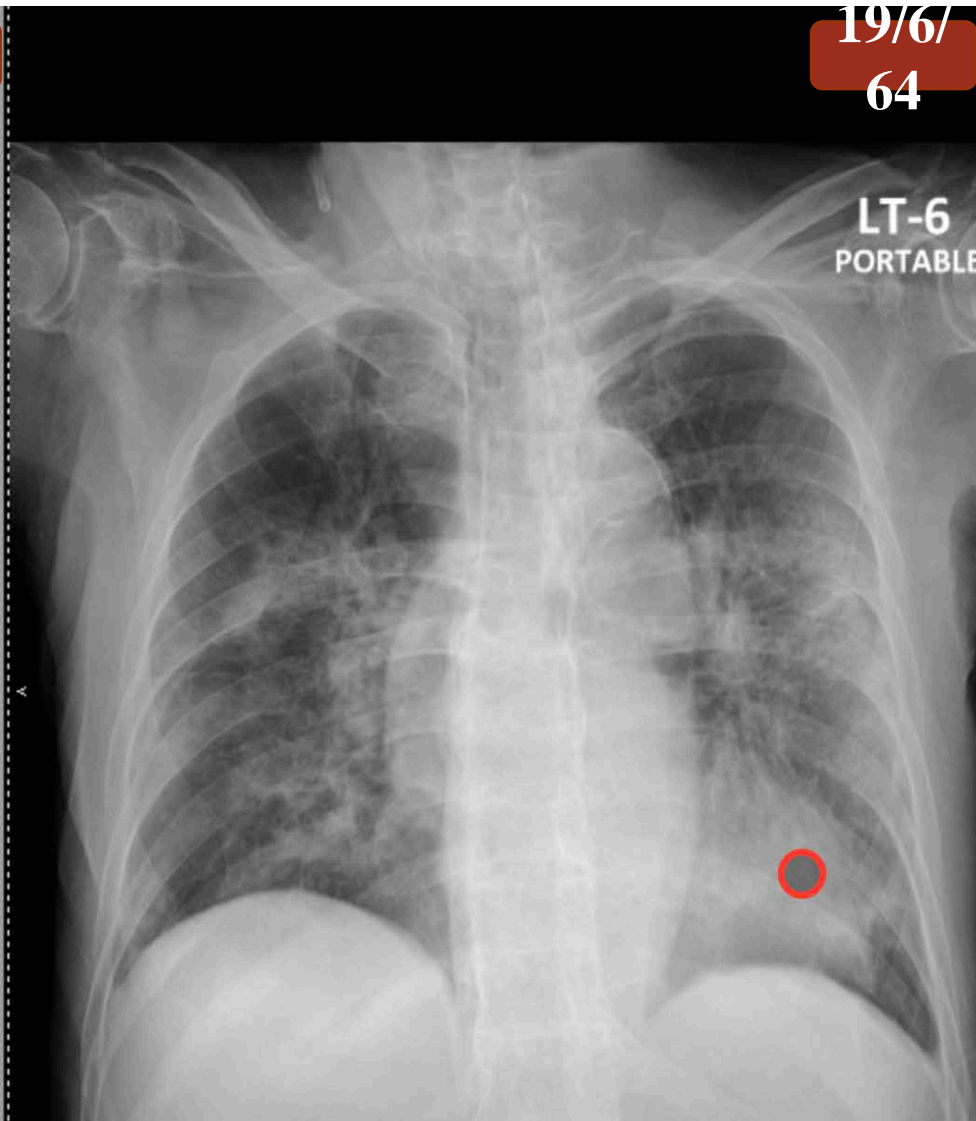
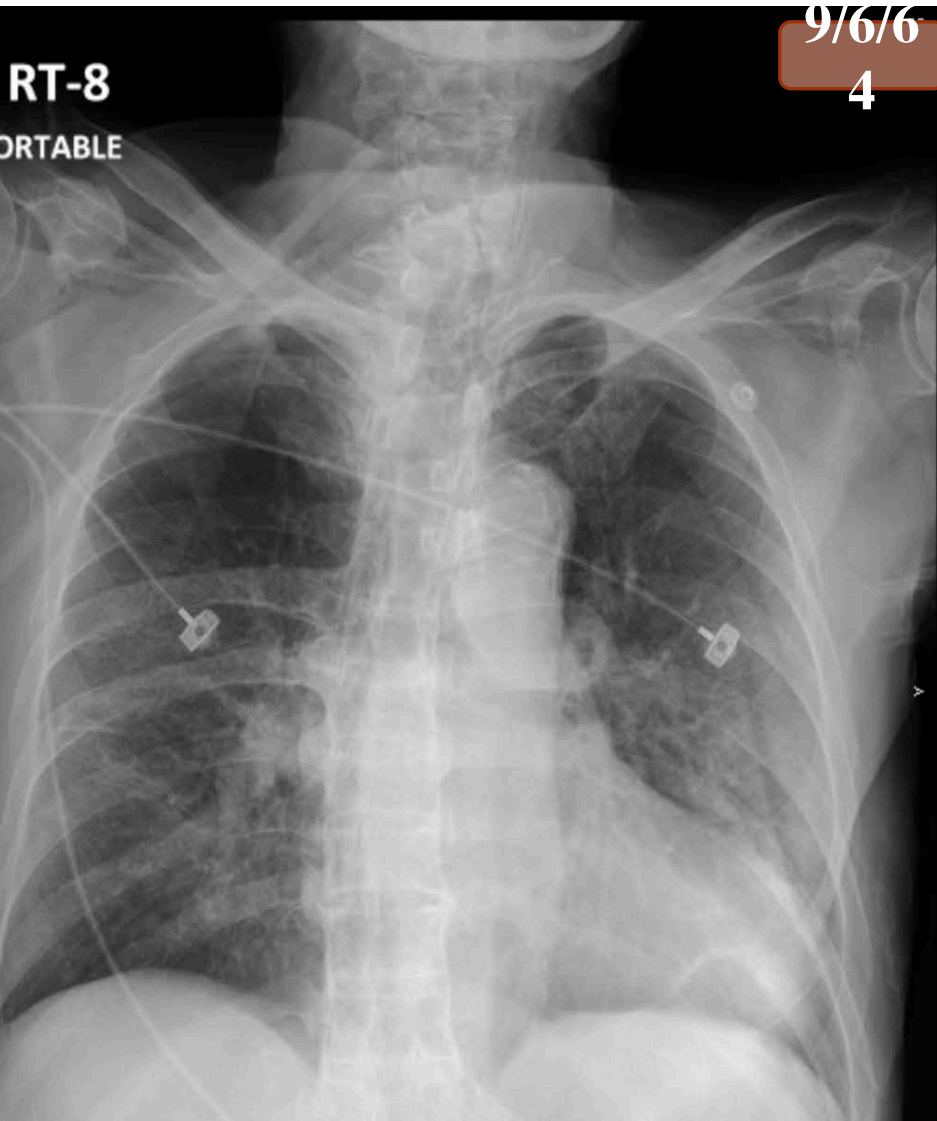
Hospital courses

- 1) **COVID-19 pneumonia – FAVI (27/5-5/6/64) + steroids (30/5-13/6/64)**
DURATION: 10 days (FAVI), 15 Days (Steroids)
- 2) Hospital-acquired pneumonia (HAP) – S/C (5/6/64, 9/6/64): *K. pneumoniae* (CREMDR) >> Rx: IV Meropenem & IV Colistin – duration 8 days
- 3) *C.difficile* infection >> Rx: oral vancomycin (15/6/64-present)
- 4) Maceration both scrota
- 5) AKI (tubuloinsterstial disease from IV colistin) with electrolyte imbalance (Na, K, Mg)



0.24 R_x - HAP. [KP, CREMR.]
 - C. difficile





Is it really safe to
discontinue isolation
precaution?

Patient Severity Classifications

Asymptomatic: No symptom

Mild Illness: Do not have shortness of breath, dyspnea and abnormal CXR

Moderate Illness: Evidence of lower respiratory tract infection with $SpO_2 > 94\%$

Critically Illness: $RR > 30/\text{min}$, $SpO_2 < 94\%$ with lung infiltration

Re-infections: Recover and had recurrent symptoms (typically more than > 6 weeks)

Duration of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infectivity: When Is It Safe to Discontinue Isolation?

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Defining the duration of infectivity of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has major implications for public health and infection control practice in healthcare facilities. Early in the pandemic, most hospitals required 2 negative RT-PCR tests before discontinuing isolation in patients with Covid-19. Many patients, however, have persistently positive RT-PCR tests for weeks to months following clinical recovery, and multiple studies now indicate that these generally do not reflect replication-competent virus. SARS-CoV-2 appears to be most contagious around the time of symptom onset, and infectivity rapidly decreases thereafter to near-zero after about 10 days in mild-moderately ill patients and 15 days in severely-critically ill and immunocompromised patients. The longest interval associated with replication-competent virus thus far is 20 days from symptom onset. This review summarizes evidence-to-date on the duration of infectivity of SARS-CoV-2, and how this has informed evolving public health recommendations on when it is safe to discontinue isolation precautions.

Keywords. SARS-CoV-2; COVID-19; transmission-based precautions; isolation.

What are evidence of safety?

- Data on viral recovery from cell culture is the proxy of transmission rate.
- In majority of patients, PCR can be recovered for several weeks, while cultures could not be identified >8 days of those cases.
- US CDC reported that they had not been able to isolate competent virus from viral culture >9 days on onset of symptoms.
- In the first COVID-19 wave, sample with Ct value > 34 was associated with undetectable viral cultures and had been used to guide for D/C isolation

Limitations of using Ct Value to help guide for D/C Isolation

Ct values must be interpreted with caution as they do not reflect a true viral load, which requires standardization using reference curves. As such, they are not directly comparable across assays [37]. Furthermore, differences in specimen collection quality and reaction conditions can introduce further variation [38, 39]. This imprecision in PCR testing is most apparent when the amount of viral nucleic acid at the sampling site approaches the limit of detection for the assay and is the most common reason for why some patients alternate between testing negative and testing positive. Lastly, only traditional real-time PCR assays produce a Ct value; assays that use isothermal amplification do not produce a Ct value and nested PCR assays are not designed for quantitative interpretation [40].

SIGNIFICANCE OF PATIENTS WHO TEST PCR-POSITIVE AFTER TESTING NEGATIVE

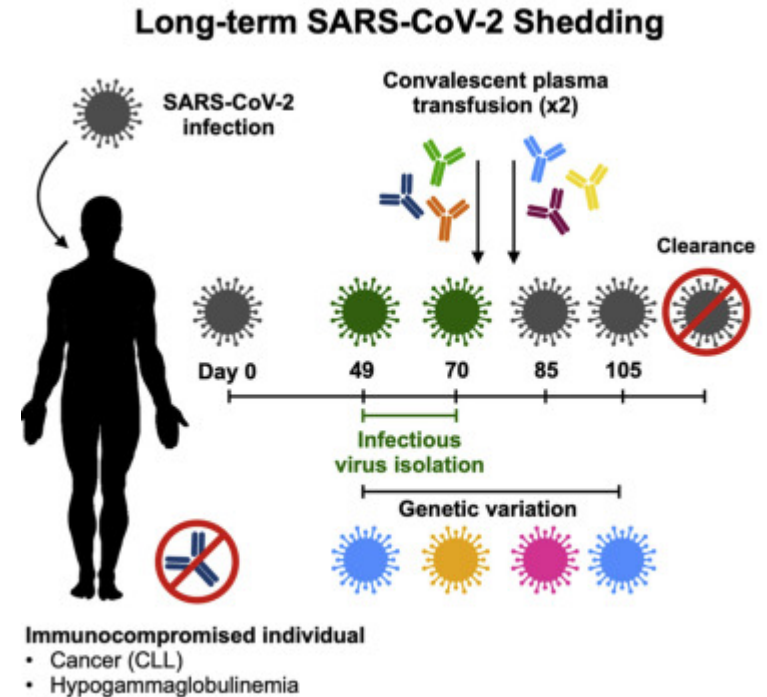
Investigators from Guangdong Province, China, analyzed 619 hospitalized patients with Covid-19 who were discharged after resolution of fever, improvement in respiratory symptoms, and 2 consecutive negative PCR samples >24 h apart on both respiratory tract and gastrointestinal tract samples [50]. All discharged cases were isolated in designated hotels, kept in observation, and retested on days 7 and 14 after recovery. 87 patients (14.1%) tested positive, of whom 77 were asymptomatic and 10 had mild cough. Viral cell culture was unsuccessful in all cases; furthermore, full-length genomes could not be sequenced in any cases, suggesting genome degradation.

Similarly, the Korean CDC reported on epidemiologic and contact tracing for 285 patients who recovered from Covid-19, tested negative, and then tested positive again by PCR [51]. On average, the re-positive test occurred 45 days after initial symptom onset (range 8–82 days). Retesting was done in 37.5% of patients because of new symptoms such as cough or sore throat. Viral cell culture testing was done in 108 re-positive cases, and all were negative. PCR Ct values were >30 in 89.5% of cases, suggesting that the negative-to-positive phenomenon represents sampling variability near the assay limit of detection. None of 790 contacts of the 285 re-positive cases (including 351 family members) developed Covid-19.

SUMMARY AND IMPLICATIONS FOR PUBLIC HEALTH RECOMMENDATIONS

In summary, based on a rapidly expanding evidence base, we currently draw the following conclusions regarding the timing and duration of SARS-CoV-2 transmissibility (Figure 1):

1. SARS-CoV-2 is most contagious right before and immediately following symptom onset.
2. Contagiousness rapidly decreases to near-zero after about 10 days from symptom onset in mild-moderately ill patients and 15 days in critically ill and immunocompromised patients. The longest duration of viral viability that has been reported thus far is 20 days from symptom onset.
3. Persistently positive SARS-CoV-2 RNA PCRs in recovered patients are common but are generally associated with high Ct values, reflecting low viral loads. These do not indicate replication-competent virus and are not associated with contagiousness.
4. PCR assays that alternate between positive and negative results in patients who have recovered from Covid-19 most likely reflect sampling variability and low levels of viral debris at the borderline of detection. These patients are unlikely to be contagious.
5. Infection confers at least short-term immunity in most cases; however, the duration of immunity is unclear and several cases of re-infection have now been confirmed.



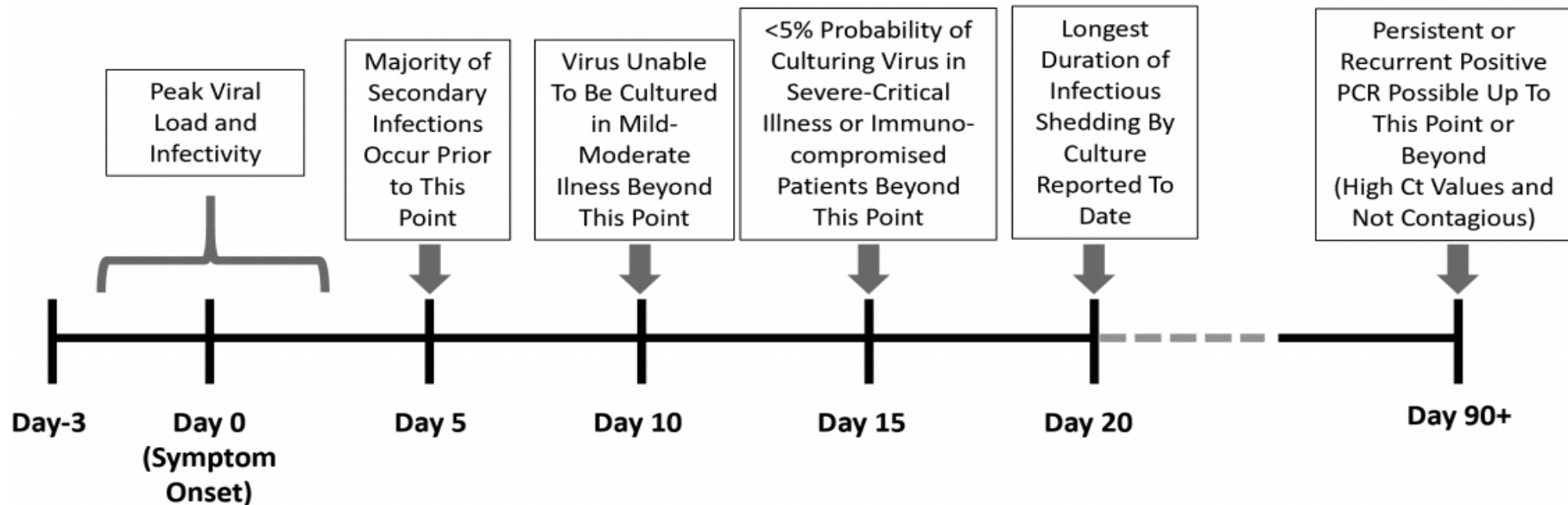


Table 2. WHO and CDC Guidance for Discontinuing Isolation in Patients with Confirmed Covid-19 Infection and Approach to Persistent or Recurrent Positive PCR Tests

Category	WHO	CDC
Symptomatic, initial infection	<ul style="list-style-type: none"> 10 days after symptom onset, plus At least 3 additional days without symptoms (fever or respiratory symptoms) 	<ul style="list-style-type: none"> <i>Mild-moderate Illness, Not Severely Immunocompromised:</i> 10 days since symptom onset + 24 h since last fever + improvement in symptoms <i>Severe-critical Illness OR Severely Immunocompromised:</i> At least 10 days and up to 20 days since symptom onset + 24 h since last fever + improvement in symptoms
Asymptomatic, initial infection	<ul style="list-style-type: none"> 10 days after positive test 	<ul style="list-style-type: none"> <i>Not Severely Immunocompromised:</i> 10 days since first positive test <i>Severely Immunocompromised:</i> At least 20 days and up to 20 days since first positive test
Recovered from Covid-19 but persistent or recurrent PCR positive	<ul style="list-style-type: none"> No specific recommendation 	<ul style="list-style-type: none"> <i>Asymptomatic:</i> Retesting not recommended within 3 months after date of symptom onset, even if the patient has close contact with an infected person. <i>Symptomatic:</i> If new symptoms develop within 3 months of initial symptom onset, and alternative etiology cannot be identified, consider retesting. Isolation may be considered in consultation with infectious disease or infection control experts, especially if symptoms developed within 14 days after close contact with an infected person.

In July and August, CDC modified their guidance to a more nuanced approach based on severity-of-illness and immunocompetence [64]. Specifically, while CDC still recommends 10 days of isolation from symptom onset (including >24 h since resolution of fever and improvement in symptoms) for mild-moderately ill patients without severely immunocompromising conditions, they now recommend at least 10 days and up to 20 days for patients with severe-critical illness or severely immunocompromising conditions. For asymptomatic patients, 10 days is recommended from the first positive PCR test (and up to 20 days for severely immunocompromised patients). Moreover, CDC recommends avoiding test-based clearance given the evidence that people with persistently positive PCR tests are not contagious. Test-based clearance should be reserved for rare cases when there is a need to discontinue isolation early, or potentially to inform a decision to prolong isolation for severely immunocompromised patients.

What you need to do, if DC Isolation?

- No need to wear PPE
- Practice Standard Precaution
- Clean environment well
- No need for RT-PCR to help guide for DC, but can be used to guide very early DC Isolation with Ct value
- Educate nurses in the unit (learn from ICU) and educate patients' relatives



แนวทางการยกเลิก **isolation** ผู้ป่วย **COVID-19** เพื่อย้ายผู้ป่วยออกจากหอผู้ป่วยโควิด19 เพื่อมาทำการรักษาต่อในหอผู้ป่วยทั่วไป ของรพ.ธรรมศาสตร์เฉลิมพระเกียรติ

1. ในผู้ป่วยที่ไม่ได้มีภูมิคุ้มกันบกพร่องรุนแรง หรือ **severe critically ill** (ดูข้อ 2 และ 3) และปัจจุบันไม่ได้รับ **high flow oxygen** แล้ว สามารถย้ายได้ หลังจากมีอาการ 14 วัน หรือ หลังจากตรวจพบเชื้อ 14 วัน โดยไม่ต้อง **swab** ซ้ำ โดยผู้ป่วยทุกรายต้องได้รับการอนุมัติจากแพทย์ผู้เชี่ยวชาญโรคติดเชื้อก่อนย้ายเสมอ
2. ในผู้ป่วยที่มีภูมิคุ้มกันบกพร่องรุนแรง เช่น เป็นมะเร็ง รับประทานยากดภูมิเป็นระยะเวลานาน หรืออื่น ๆ ตาม
วิจรรณญาณของแพทย์ผู้เชี่ยวชาญโรคติดเชื้อ สามารถย้ายได้ หลังจากมีอาการ 21 วัน หรือ หลังจากตรวจพบ
เชื้อ 21 วัน โดยต้องให้ แพทย์ผู้เชี่ยวชาญโรคติดเชื้อพิจารณาว่าควรทำ **RT-PCR** ประกอบ ก่อนย้ายผู้ป่วย
เหล่านั้น หรือไม่
3. ในผู้ป่วยที่มีอาการ **severe critically ill** สามารถย้ายได้ หลังจากมีอาการ 21 วัน หรือ หลังจาก
ตรวจพบเชื้อ 21 วัน โดยต้องให้แพทย์ผู้เชี่ยวชาญโรคติดเชื้อพิจารณาว่าควรทำ **RT-PCR** ประกอบ ก่อน
ย้ายผู้ป่วยเหล่านั้น หรือไม่

**Thank you for
your attention!**
